
Cell-cell junction remodeling in the heart: Possible role in cardiac conduction system function and arrhythmias?

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Authors: V Mezzano, F Sheikh

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Public Summary:

Considerable attention has focused on cardiac cell junction proteins, which electromechanically couple cells, since mutations/deficiencies in their components are linked with various human heart diseases. However, the underlying molecular and cellular basis for their role in disease remains unclear and understudied in humans.

Scientific Abstract:

Anchoring cell-cell junctions (desmosomes, fascia adherens) play crucial roles in maintaining mechanical integrity of cardiac muscle cells and tissue. Genetic mutations and/or loss of critical components in these macromolecular structures are increasingly being associated with arrhythmogenic cardiomyopathies; however, their specific roles have been primarily attributed to effects within the working (ventricular) cardiac muscle. Growing evidence also points to a key role for anchoring cell-cell junction components in cardiac muscle cells of the cardiac conduction system. This is not only evidenced by the molecular and ultra-structural presence of anchoring cell junctions in specific compartments/structures of the cardiac conduction system (sinoatrial node, atrioventricular node, His-Purkinje system), but also because conduction system-related arrhythmias can be found in humans and mouse models of cardiomyopathies harboring defects and/or mutations in key anchoring cell-cell junction proteins. These studies emphasize the clinical need to understand the molecular and cellular role(s) for anchoring cell-cell junctions in cardiac conduction system function and arrhythmias. This review will focus on (i) experimental findings that underline an important role for anchoring cell-cell junctions in the cardiac conduction system, (ii) insights regarding involvement of these structures in age-related cardiac remodeling of the conduction system, (iii) summarizing available genetic mouse models that can target cardiac conduction system structures and (iv) implications of these findings on future therapies for arrhythmogenic heart diseases.

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